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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SITTON, JEHANNE SOUAYA	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/007,781	BOLK ET AL.	
	Examiner	Art Unit	
	Jehanne Souaya Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20,26 and 28* is/are allowed.

6)☒ Claim(s) *19,21-25,27 and 29-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Currently, claims 19-38 are pending in the instant application. Claims 22-38 are newly added. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn. The following rejections are either newly applied or are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. Claims 19, 21-25, 27, and 29-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims broadly encompass a nucleic acid molecule comprising SEQ ID NO: 1 but wherein the nucleotide at position 3949 of SEQ ID NO: 1 is not thymidine, as well as sequences that hybridize to such, and sequences comprising sequences within SEQ ID NO: 1 including nucleotide 3949, complements of such, as well as microarrays comprising such sequences.

With regard to claim 19 and claims that depend therefrom, while the specification teaches the wildtype sequence of SEQ ID NO: 1 with a thymidine at position 3949 and teaches the identity of a variant with a G at position 3949 wherein an individual homozygous for a G at said position is protected from CAD and MI as compared to individuals with a T at this position. The specification, however, does not demonstrate possession of a variant nucleic acid molecule with an A or a C at this position nor does it teach the effect of having an A or C at said position.

With regard to claims 21, 38, and the claims that depend therefrom, the claims encompass mutants, variants, and homologs of SEQ ID NO: 1 with nucleic acid changes at different positions because the hybridization language recited in the claims does not limit the claim to the complete complement of SEQ ID NO: 1. It is clear from the recitation in the claim that nucleic acids with mismatches, additions or deletions, would be capable of hybridizing to SEQ ID NO: 1. The recitation of allele specific oligonucleotide does not structurally limit the claim. Further, sequences that can hybridize (these sequences can tolerate mismatches) to a region within SEQ ID NO: 1, wherein the region does not comprise position 3949, are also encompassed by the claimed recitation.

With regard to claim 29 and claims that depend therefrom, the claim recites "consisting of a portion of at least 10 contiguous nucleotides of SEQ ID NO: 1..." which could be interpreted a number of different ways. For example, the claims could be interpreted to encompass a nucleic acid molecule that is a portion of at least 10 contiguous nucleotides of SEQ ID NO: 1. Bu the claims could also be interpreted to encompass a nucleic acid consisting of a certain sequence, a portion, of which is 10 contiguous nucleotides of SEQ ID NO: 1. In the former case, nucleic acids smaller than 10 nucleotides in length are encompassed. In the latter

case, the recitation is analogous to a "comprising" claim. In other words, the portion has at least 10 contiguous nucleotides of SEQ ID NO: 1, but could have other sequences as well. Thus the claims are not limited to exact sequences from SEQ ID NO: 1, but to sequences that only need have 10 contiguous sequences from SEQ ID NO: 1. For example, Accession number BC012063 teaches a sequence, "a portion" from the claimed recitation, that contains a sequence complementary to positions 3940-3954 of SEQ ID NO: 1 wherein position 3949 is a G. Such sequence was not taught or described by the specification.

The recitation of the wildtype sequence of SEQ ID NO: 1 as well as the 2 mutants taught in table 2, are not representative of the large genus of mutants, variants, and homologs, as well as completely unrelated sequences, of SEQ ID NO: 1 encompassed by the claimed recitation. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1 with a T or a G at position 3949, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18

USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

4. Claims 29-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 recites "consisting of a portion of at least 10 contiguous nucleotides of SEQ ID NO: 1...". This recitation is indefinite because it is unclear what the metes and bounds of the claimed nucleic acids are. For example, the claims could be interpreted to encompass a nucleic acid molecule that is a portion of at least 10 contiguous nucleotides of SEQ ID NO: 1. The claims could also be interpreted to encompass a nucleic acid consisting of a certain sequence, a portion, of which is at least 10 contiguous nucleotides of SEQ ID NO: 1. In the former case, nucleic acids smaller than 10 nucleotides in length are encompassed. In the latter case, the

recitation is analogous to a "comprising" claim. In other words, the portion has at least 10 contiguous nucleotides of SEQ ID NO: 1, but could have other sequences as well. Such interpretations encompass very different nucleic acids. Neither the specification nor the claims make clear what is encompassed by such recitation and thus the metes and bounds of the claim are unclear.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Kazuno et al (hereinafter referred to as Kazuno; Euro. J. Cancer; vol. 35, pp 502-506, 1999).

Kazuno teaches primers specific for thrombospondin 2 (SEQ ID NO: 1) which are capable of hybridizing to SEQ ID NO: 1 wherein the nucleotide at position 3949 is a nucleotide other than thymidine (see page 503, col. 1, lines 6-8 of first full para). The recitation of "allele specific" and "probe" do not distinguish the claimed nucleic acids from the nucleic acids of Kazuno.

7. Claims 29-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank accession number AF109906 (1998) (alignment provided).

Genbank accession number AF109906 teaches a sequence "a portion" from the claimed recitation, that contains a sequence complementary to positions 3940-3954 of SEQ ID NO: 1 wherein position 3949 is a G. The accession number teaches cloning in M13 and plasmids and thus inherently teaches vectors and host cells comprising such sequence.

8. Claims 21-24, 29-30, and 35-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Fodor et al (hereinafter referred to as Fodor; US Patent 6,582,908; 102(e) date is: 3/6/2000).

Fodor teaches and claims an array of all possible 10 mers. The instantly claimed microarray reads on the array claimed by Fodor (see Fodor, claim 15). The instantly claimed nucleic acids read on the isolated nucleic acids of Fodor. It is noted that claims 29 and 30 has been interpreted to encompass a 10mer of SEQ ID NO: 1 that includes position 3949. The term "allele specific", "probe" and "primer" do not distinguish the instantly claimed nucleic acids from the teaching of Fodor.

9. Claims 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796 12/1995).

Claims 29 and 30 have been broadly interpreted to encompass an isolated nucleic acid that is a portion of at least 10 contiguous nucleotides of SEQ ID NO: 1 wherein position 3949 is a G. Brennan teaches an array of all possible 3mer isolated nucleic acids (see Fig 1b). The claims thus encompass the sequence CGC, which is taught by Brennan.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kazuno in view of Brennan.

Kazuno teaches primers specific for thrombospondin 2 (SEQ ID NO: 1) which are capable of hybridizing to SEQ ID NO: 1 wherein the nucleotide at position 3949 is a nucleotide other than thymidine (see page 503, col. 1, lines 6-8 of first full para). The recitation of "allele specific" and "probe" do not distinguish the claimed nucleic acids from the nucleic acids of Kazuno. Kazuno does not teach these sequences on an array, however, Brennan teaches placing sequences on an array for the purposes of detecting target oligonucleotides (see col. 1, lines 16-24). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide the sequences of Kazuno on an array as taught by

Brennan for the obvious improvement of making detection of the thrombospondin 2 gene easier to perform.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Claims 20, 26, and 28 are free of the cited prior art.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name. It is also noted that

after January 12, 2004, the examiner will be located at the new USPTO campus and will be reachable at telephone number (571) 272-0752.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Sitton

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634
1/5/04